

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number  
**WO 2004/018681 A3**

(51) International Patent Classification<sup>7</sup>: C12N 15/24,  
C07K 14/54, A61K 38/20, C07K 16/24, C12N 15/62

(21) International Application Number:  
PCT/EP2003/008701

(22) International Filing Date: 6 August 2003 (06.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
02291996.3 8 August 2002 (08.08.2002) EP  
60/475,881 5 June 2003 (05.06.2003) US

(71) Applicant (for all designated States except US):  
CYTHERIS [FR/FR]; 21, rue Aristide Briand, F-92170  
Vanves (FR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MORRE, Michel,  
Christian [FR/FR]; 67, rue Nationale, F-92100 Boulogne  
Billancourt (FR). ASSOULINE, Brigitte [FR/FR]; 12/14,  
rue Sébastopol, F-92400 Courbevoie (FR). CORTEZ,  
Pierre [FR/FR]; 17, rue des Grands Augustins, F-75006  
Paris (FR). GREGOIRE, Anne [FR/FR]; 1, rue des  
Morillons, F-7015 Paris (FR).

(74) Agents: BECKER, Philippe et al.; Cabinet Becker et As-  
sociés, 35, rue des Mathurins, F-75008 Paris (FR).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,  
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,  
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
1 April 2004

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: IL-7 DRUG SUBSTANCE, IL- 7 COMPRISING COMPOSITION, PREPARATION AND USES THEREOF

(57) Abstract: The present invention relates, generally, to the fields of immunology and molecular biology. The invention discloses, more particularly, new and improved interleukin-7 drug substances, corresponding specific immunoreactive antibodies, as well as compositions comprising the same, their preparation and uses. The invention also discloses methods to characterize the impurity profile of a r-hIL-7 drug substance used for therapeutic purpose, as well as optimized nucleotide sequences encoding mammalian IL-7, recombinant expression vectors and methods for preparing and purifying said polypeptides. The present invention stems from the unexpected discovery that the long term activity of recombinant IL-7 is mostly expressed by a specific conformer and that other conformers, potential product-related substances, product-related impurities, and process-related impurities, which would normally be included in the specification of the drug substance and/or drug product, although bioactive, should be strictly minimized because they are able to trigger an immune reaction against the desired IL-7 molecule.

WO 2004/018681 A3